

# Sensitisation to Ambrosia in Switzerland: a public health threat in waiting

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## Summary

**Background:** *Ambrosia artemisiifolia* (short name = Ambrosia common ragweed) pollen is a potent allergen and has recently been found in Switzerland, spreading from the southwest of the country. The aim of this study is to describe Ambrosia sensitisation rates in the population-based SAPALDIA cohort (Swiss Study on Air Pollution And Lung Diseases In Adults) and to test whether an increase in these rates could be observed.

**Methods:** Among the 6345 participants from 8 areas who provided blood samples in 1991 and 2002, 5823 had valid results for specific IgE against common inhalant allergens tested with Phadiatop®. In 2002 Ambrosia sensitisation was measured and positive tests were analysed for *Artemisia vulgaris* (mugwort). Blood samples taken in 1991 in Ticino and Geneva were also tested for Ambrosia.

**Results:** Sensitisation rate (Phadiatop®) did not increase significantly between the two surveys and sensitisation was found in 30% of the partici-

pants. A proportion of 7.9% showed specific IgE to Ambrosia pollen. The sensitisation rate in Lugano and Geneva had not changed substantially since 1991. Among those sensitised to Ambrosia 82% also showed specific IgE against Artemisia, suggesting a high rate of cross-reactivity. Only 1.3% were sensitized to Ambrosia alone. The incidence of asthma or hay fever in participants with specific IgE to Ambrosia pollen was not higher than in the general study population.

**Conclusion:** Currently Ambrosia pollen does not appear to be an important cause of inhalant allergies in Switzerland. Sensitisation rates are low and have not increased since 1991. Due to cross-reactivity Ambrosia sensitisation may be a consequence of primary sensitisation to Artemisia. Elimination of Ambrosia plants is nevertheless mandatory to avoid a future increase.

**Key words:** allergy; Ambrosia; Artemisia; hay fever; cross-reactivity; sensitisation

## Introduction

*Ambrosia artemisiifolia* (short name Ambrosia or common ragweed) pollen may produce major hay fever symptoms during its pollination period in late summer and autumn. It has been accused of being one of the strongest sensitising pollens [1] in various countries [2]. In Switzerland, Ambrosia has spread from the areas of Geneva and Ticino in recent years and has been observed to a minor extent in many regions [3, 4]. Concern has therefore been expressed regarding potential sensitisation to Ambrosia pollen in the population and its possible increase in recent years [5].

SAPALDIA (Swiss Cohort Study on Air Pol-

lution and Lung Diseases in Adults) was initiated in 1991 with the primary aim of investigating the impact of air pollution on respiratory health [6]. The data collected also made it possible to study allergic sensitisation rates in the Swiss population. Several publications have described the prevalence of sensitisation to various respiratory allergens and influencing factors in the Swiss population [7-9] and in Europe [10, 11]. The same subjects were invited for a second examination in 2002 [12, 13]. In view of the increase in Ambrosia pollen it was decided in 2002 to specifically test sensitisation to Ambrosia pollen in this study pop-

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ulation. Initially and in 2002, the participants were tested with Phadiatop® (Phadia Uppsala Sweden) which contains a mixture of common respiratory allergens, including *Artemisia vulgaris* (short name Artemisia or mugwort) which may show cross-reactivity with Ambrosia [14]. A high level of cross-reactivity between the allergens of these two pollens has been demonstrated on a molecular level analysing the three-dimensional structure [1] and with very recently introduced molecular array techniques [15]. However, co-sensitisation, i.e., independent sensitisation to either allergen, is possible [16].

Highest pollen counts have been reported in the southern part of Switzerland (Ticino) and in

the area of Geneva. While in Geneva an increase in pollen load has been described since 1993 [3], this trend was not observable in Ticino [17]. Long-distance transport of Ambrosia pollen from France and Italy seems to play an important role in Switzerland, but pollens are also produced locally [18]. Systematic monitoring has been introduced in Ticino and Geneva [4].

Thus it was also decided to test the frozen serum samples taken in 1991 from SAPALDIA participants in Geneva and Lugano (Ticino) for IgE to Ambrosia and Artemisia, and to compare the longitudinal changes in these sensitisations in two potentially exposed populations.

## Methods

The eight study areas (Geneva, Basel, Lugano, Aarau, Wald, Payerne, Davos, Montana) were chosen to represent the variety of environmental conditions in respect of geography, climate, degree of urbanisation and air pollution in Switzerland. From the local registries of inhabitants of these areas random population samples of persons aged 18–60 years, having resided in the respective area for at least three years, were then drawn [6].

In 1991, blood samples were taken from the participants and serum samples were stored at  $-20^{\circ}\text{C}$  before despatch to the laboratory for testing. Total serum IgE was measured using the Pharmacia CAP FEIA system and the presence of specific serum IgE antibodies to a mixture of relevant respiratory allergens (pollen, house dust mites, moulds and animal epithelia) was assessed by the Phadiatop® test (Phadia Uppsala Sweden) [14]. Positive reaction was defined as proposed by the manufacturer. All serum testing for IgE was done in the Allergy Laboratory of the Department of Dermatology, University Hospital Zurich in 1993. Blood samples of two volunteers (both consistently Phadiatop® positive) were used as quality control.

In 2002 blood samples were again taken from the same individuals and stored at  $-80^{\circ}\text{C}$ . The same technicians in the same laboratory analysed these samples with the same methods between June 2005 and November 2007. The analysis included total IgE and Phadiatop®. Ambrosia was tested in all samples except from the ones of the two alpine regions of Davos and Montana (in which Ambrosia had not been observed) and Artemisia was tested if there was a positive result to Ambrosia. For both allergens the commercial assay (Immuno CAP Pharmacia) was used.

The results are reported as absolute and relative frequencies (or percentages). Exact 95% confidence intervals of proportions were computed. Changes in prevalence were assessed using the McNemar test and confidence intervals of these changes were computed based on the proportion of converters from – to + among all converters, while the number of converters was assumed to be fixed. All tests were two-tailed at a significance level of 0.05. Statistical analyses were done using SAS Version 9.1.

## Results

Table 1 shows the total number of subjects whose serum could be analysed in the cohort in 1991 and 2002 for the different areas. A total of 5823 persons provided interpretable results in both instances. Of these, 4774 subjects had Ambrosia measurements in 2002, and 375 of them showed a positive test result. Artemisia was tested in 327 of these subjects. In addition, 1093 old sera (i.e., from 1991) of participants from Lugano and Geneva were also tested for Ambrosia. 111 of these sera were positive and 108 of them were additionally tested for Artemisia.

### Sensitisation to respiratory allergens

Figure 1 shows that in most places the proportion with a positive reaction to some respiratory allergen(s) contained in Phadiatop® remained remarkably similar between the two surveys.

Overall, the sensitisation rate increased from 29.3% in 1991 to 30.3% in 2002 ( $p = 0.015$ , 95%-CI of change = [0.2–1.9%]). In Basel the sensitisation rate increased from 34.7 to 37.5% ( $p = 0.013$ , 95%-CI of change = [0.6% to 4.8%]). The proportion with positive reactions in both instances varied between 31% (Basel) and 18% (Payerne), whereas the number of converters from positive to negative was largest in Geneva and of converters from negative to positive in Lugano. There was no clear change in reactivity to respiratory allergens over this period of time; however, between 3 and 6% of the population lost their sensitisation, while between 5 and 7% newly tested positive to Phadiatop®. New positivity was mainly found in younger age groups, whereas decline in reactivity was more frequent in older subjects; thus the transition probabilities from positive to negative are

**Table 1**

Number of samples tested by study area with valid results.

	Participants with blood samples	Phadiatop® measurement	Ambrosia measurements (2002)	Ambrosia measured in both surveys	Artemisia measurements*
Basel	806	778	778	nm**	74 (698)
Wald	1178	1097	1095	nm	62 (1010)
Davos	513	460	3	nm	nm
Lugano	870	743	741	698	1991:65 (480) 2002:48 (689)
Montana	610	587	nm	nm	nm
Payerne	856	811	810	nm	40 (761)
Aarau	981	949	949	nm	74 (870)
Geneva	531	398	398	393	1991:43 (251) 2002: 29 (365)
Total all areas	6345	5823	4774	1091	1991: 108 (731) 2002: 327 (4393)

\* Artemisia was tested in Ambrosia-sensitive subjects only. In parentheses: number of subjects categorised as “non-sensitised to Artemisia” based on their negative Phadiatop test result

\*\* nm = not measured

high in older persons, whereas the younger age groups have a greater probability of becoming newly sensitised to inhalant allergens (table 2).

### Ambrosia sensitisation

Table 3 shows that between 6% (Payerne) and 10% (Basel) of the population are sensitised to

Ambrosia. The proportion of those sensitised to Ambrosia but not to Artemisia varies between 1 and 2%, with Basel also having the highest positivity rate for Ambrosia (2.1%) in this analysis. As Ambrosia was still rare in Switzerland in 1991 it is particularly interesting to examine the evolution between 1991 and 2002.

**Table 2**

Transition probabilities in different age groups for Phadiatop® in the SAPALDIA population (1991–2002).

Age category SAPALDIA (1991)	Probability of newly acquired Phadiatop® positivity* <sup>a</sup>	Probability of lost Phadiatop® positivity** <sup>a</sup>
<30	0.107 (0.084–0.133)	0.111 (0.083–0.144)
30–40	0.090 (0.073–0.110)	0.126 (0.097–0.160)
40–50	0.074 (0.061–0.090)	0.175 (0.141–0.213)
>50	0.057 (0.044–0.072)	0.222 (0.180–0.269)
trend test	p <0.0001	p <0.0001

\* Among subjects with a negative Phadiatop® test in 1991; \*\* Among subjects with a positive Phadiatop® test in 2002; <sup>a</sup> In parentheses: 95%-confidence intervals

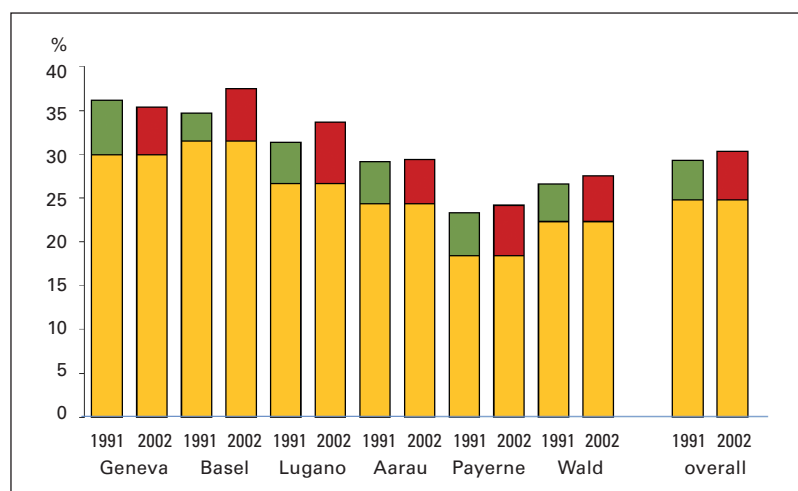
### Evolution of Ambrosia sensitisation

In view of the longer presence and higher pollen load of Ambrosia in Geneva and Lugano (Ticino) as compared to other areas of Switzerland, we used the cohorts of these two areas to test whether an increase in Ambrosia sensitisation could be observed. Data from 1091 subjects could be used for this purpose (see table 1) and 1082 individuals also provided valid results for Artemisia.

Table 4 shows the evolution between the two examinations in the populations from Geneva and Lugano (Ticino). Subjects with sensitisation to Ambrosia but not Artemisia (i.e., who must be specifically sensitised to Ambrosia) made up 1.1% of the population in 2002 and 1.9% in 1991. A new positivity to Ambrosia alone was observed only in 3 individuals (0.3%) and new sensitisation to Ambrosia and Artemisia in 1.1%. Thus a maximum of 14 persons (1.4%), might have been newly sensitised to Ambrosia in 11 years. At the same time 44 (4.0%) persons who tested positive to one of the two allergens in 1991 where no longer sensitised in 2002. This development did not show any significant differences between the two areas (data not shown).

### Symptom development in persons with positive Phadiatop® and/or Ambrosia reactions

To determine whether Ambrosia sensitised persons have a higher probability of developing asthma or hay fever, we compared the incidence of these two conditions across the four subgroups with distinct patterns of sensitisation to Phadiatop® and Ambrosia (i.e., +/+, +/-, -/+ and -/-) in persons from Lugano and Geneva who did not have physician-diagnosed asthma in 1991 (N =

**Figure 1**

Rates of sensitisation to Phadiatop® in the two surveys (1991 and 2002). Yellow segments: Phadiatop® positive in both surveys; green segments: converters from positive to negative; red segments: converters from negative to positive.

1030) or symptoms of hay fever (defined as a self-reported hay fever for the year of the study or the year before, N = 942). Table 5 shows that there was no relevant difference in asthma evolution

between the groups and that the rate of new hay fever did not statistically differ between the three groups of subjects with any form of sensitisation.

## Discussion

Sensitisation to Ambrosia pollen has attracted considerable attention in Switzerland and elsewhere in recent years, and several publications have suggested that Ambrosia may become an important hazard for asthmatics in Switzerland as in other affected areas with high plant counts [5], such as Italy [19]. It has been postulated that already an Ambrosia pollen load of more than 11 pollen/m<sup>3</sup> air can lead to allergic symptoms [20]. This pollen amount has been repeatedly exceeded

in Switzerland in recent years in parts of the canton Ticino and almost attained in the Geneva area [21].

In this study we were not able to confirm an increase in Ambrosia sensitisation in the populations examined. However, observations and experience from other countries with a high Ambrosia load should prompt us to keep a watch on this plant [22]. In Switzerland Artemisia is widespread and sensitisation to its pollen is cur-

**Table 3**

Ambrosia and Artemisia sensitisation in the SAPALDIA areas\* in 2002.

Area	Total tested for Ambrosia	Ambrosia positive & Artemisia positive		Ambrosia positive & Artemisia negative		Total Ambrosia positive**	
		N	% <sup>a</sup>	N	%	N	% <sup>a</sup>
Basel	778	58	7.5 (5.7–9.5)	16	2.1 (1.2–3.3)	80	10.3 (8.2–12.6)
Wald	1095	48	4.5 (3.2–5.8)	14	1.3 (0.7–2.1)	85	7.8 (6.2–9.5)
Lugano	741	39	5.3 (3.8–7.1)	9	1.2 (0.6–2.3)	51	6.9 (5.2–9.0)
Payerne	810	33	4.1 (2.8–5.7)	7	0.9 (0.3–1.8)	47	5.8 (4.3–7.6)
Aarau	949	64	6.8 (5.2–8.5)	10	1.1 (0.5–1.9)	79	8.3 (6.6–10.3)
Geneva	398	25	6.3 (4.1–9.1)	4	1.0 (0.3–2.6)	33	8.3 (5.8–11.4)
Total	4771	267	5.7 (5.0–6.3)	60	1.3 (0.9–1.6)	375	7.9 (7.1–8.7)

\* Montana and Davos excluded.

\*\* Numbers exceed the sum of the N's of the subcategories defined by Artemisia sensitisation status since some subjects who were sensitised to Ambrosia had missing or invalid data on Artemisia sensitization.

<sup>a</sup> Percentages with 95%-confidence intervals.

**Table 4**

Development of Ambrosia sensitisation between 1991 and 2002 (Geneva and Lugano only).

SAPALDIA 2002				
		Ambrosia negative	Ambrosia positive and Artemisia negative	Ambrosia positive and Artemisia positive
SAPALDIA 1991	Ambrosia negative	966 (98.6%)	3 (0.3%)	11 (1.1%)
	Ambrosia positive and Artemisia negative	14 (66.7%)	2 (9.5%)	5 (23.8%)
	Ambrosia positive and Artemisia positive	30 (37.0%)	7 (8.6%)	44 (54.3%)
	Total Ambrosia tested	1010 (93.3%)	12 (1.1%)	60 (5.5%)
				Total Ambrosia tested
				1082 (100%)

Red shaded: positive converters, i.e., subjects having become newly IgE positive (sensitised) between 1991 and 2002

Green shaded: negative converters, i.e., subjects having become IgE negative (lost sensitisation) between 1991 and 2002

**Table 5**

Incidence of asthma and hay fever in different groups of subjects with distinct sensitisation patterns at baseline (areas Lugano and Geneva).

	New cases of hay fever*	No new hay fever	Total	New cases of asthma*	No new asthma	Total
Phadiatop® neg. and Ambrosia neg.	38 5.2% (3.7–7.1)	690 94.8%	728 77.3%	14 2.0% (1.1–3.3)	703 98.0%	717 (69.6%)
Phadiatop® pos. and Ambrosia neg.	28 17.1% (11.7–23.7)	136 82.9%	164 17.4%	15 6.8% (3.9–11.0)	205 93.2%	220 (21.4%)
Phadiatop® neg. and Ambrosia pos.	0 0% (0–77.6)	2 100%	2 0.2%	0 0% (0–63.2)	3 100%	3 (0.3%)
Phadiatop® pos. and Ambrosia pos.	13 27.1% (15.3–41.8)	35 72.9%	48 5.1%	7 7.8% (3.2–15.4)	83 92.2%	90 (8.7%)
Total	79 8.4% (6.7–10.3)	863 91.6%	942 100%	36 3.5% (2.5–4.8)	994 96.5%	1030 (100%)

\* Absolute frequency and row percentage (with 95% confidence interval in parentheses)



rently more prevalent and more widespread than to Ambrosia.

However, the potential cross-reactivity between allergens of these two pollens may render patients initially sensitised to *Artemisia* pollen sensitive to Ambrosia as well. Unfortunately we are unable to distinguish between the two sensitisations, but our results allow the speculative conclusion that the observed sensitisation to Ambrosia in Switzerland may so far have in large part been due to primary sensitisation to *Artemisia* leading by cross-reactivity to sensitisation against Ambrosia.

For this reason future preventive campaigns may need to warn allergic individuals against both Ambrosia and *Artemisia*. Patients with inhalant allergies should be aware that sensitisation to *Artemisia* may at a later stage develop into an allergy against Ambrosia, and that therefore exposure to *Artemisia* should also be avoided.

In general, no increase in sensitisation to respiratory allergens could be observed in our study populations or in those with potential exposure to *Artemisia* pollen. The apparent decrease in sensitisation is partially explained by the increasing age of the population studied and the concomitant increased probability of losing sensitisation. This is consistent with the findings of the ECRHS study, which suggest that the widely observed upward trends in sensitisation rates across Europe may essentially reflect a cohort phenomenon [23]. In this regard further observations are needed.

In any case, our results do not support the notion that Ambrosia plants and pollen are already an important cause of inhalant allergies in Switzerland at present and therefore do not yet represent an important public health issue. Our results documenting low Ambrosia sensitisation rates in 1991 and also in 2002 further suggest that the feared rise in sensitisation to Ambrosia has not yet occurred. Campaigns to eliminate Ambrosia wherever possible are nevertheless mandatory, to avoid a further spread of Ambrosia which could involve very severe and widespread allergies as observed in Hungary, Italy or France in recent decades.

In summary, our results document low Ambrosia sensitisation rates in 1991 and in 2002, even in areas with a significant Ambrosia pollen load, strongly suggesting that the feared rise in

sensitisation to Ambrosia has not yet taken place. To the best of our knowledge the situation has not dramatically changed in the meantime: thus the situation provides a not-to-be-missed window of opportunity for the introduction of effective preventive measures.

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